Serologic detection and quantification of hepatitis B core antigen

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The official link for this solicitation is: https://sbir.nih.gov/sites/default/files/PHS2016-1.pdf

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Description:

Background

Hepatitis B is a major public health problem in United States, where 1.4 million persons are estimated to be infected with the virus. HBV surface antigen (HBsAg) is the mainstay serological marker used for identifying HBV infection and evaluating the efficacy of antiviral therapy. However, it is not a reliable marker of HBV found in blood, as it is shed from the liver in much greater abundance than HBV virions. Further, HBsAg can be shed from HBV even when it is residing in the liver in the latent (non-replicating) state.

HBV core antigen (HBcAg) is a constituent of the HBV nucleocapsid, which after encapsidation is released into the circulation. HBcAg in serum or plasma is a better indicator than HBsAg of the extent of shedding of HBV virions from the liver to peripheral blood, i.e., ‘productive’ HBV infection. Critically, as transcription and translation of HBcAg production are not inhibited by nucleotide analogues currently used for antiviral therapy, patients treated with these drugs continue to produce HBcAg for considerable periods of time. Immunoassays to detect HBcAg can therefore help in identifying HBV infections without resorting to HBsAg or HBV DNA testing.

Previous studies have shown that HBc antigenimia correlates positively with HBcAg production in the liver. Several methodologies for the detection of HBcAg core antigen in serum have been published but assays for its detection and quantification are not commercially available for use in diagnostic procedures. Development of a reliable immunoassay that can also be an alternative to HBsAg and HBV DNA testing, is needed.

Project Goals

- Identify a panel antibodies that have the potential to detect HBV core antigen in clinical samples.
- Validate and develop a serological assay for quantitative detection of HBV core antigen
- Validate the performance characteristics of the assay using commercial panels of serum samples from HBV-infected persons.
- Validate the performance characteristics of the assay using with prospectively obtained serum samples from HBV-infected persons.
- Establish protocols to scale up production of validated assay.

Phase I Activities and Deliverables

Deliverable: Design and develop a simple immunoassay for detection and quantification of HBcAg in human serum or plasma from persons with acute and chronic HBV infection

Activity: Identify a panel of antibodies with the potential to be capture agents for HBcAg in serum or plasma.

Projected Phase II Activities

Deliverable: Optimize and validate the assay using clinical samples from HBV infected patients and controls

Activity: Establish sensitivity and specificity of the assay, continue to refine the assay and improve performance characteristics of the assay

Deliverable: Establish and validate prototype assay.

Deliverable: Produce final report and explore feasibility of transferring technology to commercial and state and public health laboratories.

Impact

Serologic testing for hepatitis C virus (HCV) core antigen is increasingly being used to identify persistent HCV infection and evaluating the efficacy of anti-HCV therapy. Similarly, testing for HBcAg has potential for use to identify productive HBV infection and evaluating the efficacy of anti-HBV therapy. Worldwide more than 350 million people are chronically infected with HBV. Improved antivirals are in the pipeline that potentially cure instead of suppress HBV. In the next 5-10 years, a substantial proportion of HBV-infected persons can then benefit from access to testing for HBVcAg. This start- up initiative, when funded and successfully developed, should lead to a marketable product for use in commercial and publically funded diagnostic laboratories.

Commercialization Potential

A simple assay for serologic detection and quantification of Hepatitis B virus core antigen with high sensitivity and specificity and low cost can lead to a marketable product for use in commercial and publically-funded diagnostic laboratories. The market potentially comprises the 350 million people

who are chronically living with HBV worldwide.

National Center for Immunization and Respiratory Diseases (NCIRD)

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